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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/945,376 | 08/31/2001 | Pedro A. Navarro Acevedo | 35718/237948(5718-140) | 2174 |

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| EXAMINER |
|---|
| KUBELIK, ANNE R |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1638 | |

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/945,376 | ACEVEDO ET AL. | |
| | Examiner | Art Unit | |
| | Anne R. Kubelik | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on 16 December 2002 .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-38 is/are pending in the application.

4a) Of the above claim(s) 18-38 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

1. Applicant's election of Group I (claims 1-17) in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The restriction is made FINAL. Claims 18-38 are withdrawn from consideration as being drawn to non-elected inventions.

2. Paper No. 5, filed 23 January 2002, states that an information disclosure statement was filed. However, this information disclosure statement fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office. No form 1449 was filed by Applicant. The references have been placed in the application file, but the information therein has not been considered.

3. The disclosure is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code. See pg 11, line 28. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Sequence identifiers are missing from pg 28, lines 6, 12 and 13.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these

requirements in the time period set forth in this Office action will be held to be non-responsive.

5. The title of the invention is not descriptive of the instant invention, which is a pathogen-activated promoter, plants transformed with constructs comprising it and methods of using it to express heterologous nucleic acids. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

6. The abstract is not descriptive of the instant invention, which is a pathogen-activated promoter, plants transformed with constructs comprising it and methods of using it to express heterologous nucleic acids. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

7. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because non-initialed and/or non-dated alterations have been made to the oath or declaration. For the first inventor, a date was changed and for the fourth inventor the citizenship was changed. See 37 CFR 1.52(c).

***Claim Objections***

8. Claims 1-2, 5, 9, 13 and 17 are objected to because of the following informalities:

In claim 1, part (a), --SEQ ID-- should be inserted before "NO:3".

In claim 1, part (b), the second "nucleotide" should be plural.

There is an improper article before "sequence of" in claim 1, part (c), claim 5, part (c), claim 9, part (c), and claim 13, part (c), and before "nucleotide" in claim 2, line 1.

In claim 5, part (a), "SEQNO:3" should be replaced with --SEQ ID NO:3--.

In claim 17, "claims" should be singular.

### *Claim Rejections - 35 USC § 112*

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to promoters that hybridize to SEQ ID NO:3 or that comprise 30 contiguous nucleotides of SEQ ID NO:3, constructs comprising those promoters operably linked to heterologous genes, cells and plants comprising the constructs, and methods of using them to induce expression of heterologous genes.

The instant specification, however, only provides guidance for transformation of maize and soybean with the maize latex protein gene (Zm-MLP1) via particle bombardment and *Agrobacteria* (examples 1-3); transformation of maize with ERE-avrRxv, which places control of transcription of the avrRExv gene of the estrogen receptor mRNA (example 4); and

abundance profiling of mRNAs upregulated by induction to avr gene expression to show that Zm-MLP1 is upregulated (example 5). The Zm-MLP1 coding sequence is SEQ ID NO:1, which encodes SEQ ID NO:2; the promoter is SEQ ID NO:3.

The instant specification fails to provide guidance for how Zm-MLP1 and its promoter were isolated. The instant specification also fails to provide guidance for exact hybridization or amplification conditions and probes/primers to use in isolation of promoters other than SEQ ID NO:3. The specification fails to teach any 30 contiguous nucleotide segments of SEQ ID NO:3, or segments of any other size, that have promoter activity. The specification also fails to provide evidence that SEQ ID NO:3 functions as a promoter.

Thirty base-pair long regions of a DNA fragment that has promoter activity cannot predictably be assumed to also have promoter activity. Deletion analysis of various promoters have shown that even DNA segments from the portion of a promoter region containing sequence elements thought to be most important (*e.g.*, the TATA-box) need to be longer than 30 basepairs. Maiti et al (1997, Transgen. Res., 6:143-156), in studies on a figwort mosaic virus promoter, found that smallest portion upstream of the transcriptional start site of that would support transcription was 198 basepairs long; segments of 73 and 37 basepairs did not work (Fig. 4). Doelling et al (1995, Plant J. 8:683-692) found that the minimal rRNA promoter of *Arabidopsis thaliana* is at least 33 nucleotides long (Fig. 1). The instant specification fails to teach any 30 contiguous nucleotides of SEQ ID NO:3 that have promoter activity.

Identification of the functional parts of promoters is unpredictable. Chen et al (2000, Sex. Plant Reprod. 13:85-94) teach that two promoters with similar expression patterns have

major differences in the expression elements required for expression in various flower parts (pg 92, right column, last two paragraphs).

The region of a given promoter that has a specific activity cannot be predicted and involves the complex interaction of different subdomains (Benfrey et al, 1990, Science 250:959-966, see Abstract, Fig. 3-5). Even a very small region may be critical for activity, and the criticality of a particular region must be determined empirically (Kim et al, 1994, Plant Mol. Biol. 24:105-117, Tables 1-4, Abstract, Fig. 1-2).

Mutation of promoter sequences also produces unpredictable results. Donald et al (1990, EMBO J. 9:1717-1726) in a mutational analysis of the *Arabidopsis rbcS-1A* promoter found that the effect of a particular mutation was dependent on promoter fragment length (paragraph spanning pg 1723-1724).

As the specification does not describe the transformation of any plant with a promoter that hybridizes to SEQ ID NO:3 or comprises any 30 nucleotide fragment of SEQ ID NO:3, wherein the promoter is operably linked to a heterologous nucleic acid, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those that express the heterologous nucleic acid, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled.

11. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of promoters that hybridize to SEQ ID NO:3 or that comprise 30 contiguous nucleotides of SEQ ID NO:3 and their use. In contrast, the specification only describes a putative promoter that comprises SEQ ID NO:3. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided. Applicant does not describe the claimed 30 contiguous nucleotide fragments or promoters that hybridize to SEQ ID NO:3

Hence, Applicant has not, in fact, described DNA molecules that promoters that hybridize to SEQ ID NO:3 or that comprise 30 contiguous nucleotides of SEQ ID NO:3, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus

> that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 1, part (c), claim 5, part (c), claim 9, part (c), and claim 13, part (c) are indefinite in their recitation of "stringent conditions". It is unclear what conditions are considered stringent. Thus, the metes and bounds of the claimed nucleic acid are unclear.

Claim 12 lacks antecedent basis for the limitation "The plant of claim 9" as claim 9 is drawn to a plant cell.

It is unclear in claim 17 if the seed has been transformed with the DNA construct or if it has been transformed with some other nucleic acid. Note that not all seed produced by a transformed plant will comprise the nucleic acid with which the parent plant has been transformed. If Applicant wishes to claim a seed transformed with the DNA construct, it is

suggested that --, wherein the seed comprises the DNA construct-- be inserted after "13".

***Claim Rejections - 35 USC § 102***

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 1-5, 8-9, 12-13 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Stalker et al (WO 98/30698).

Stalker et al teach a cotton promoter comprising 41 contiguous nucleotides of SEQ ID NO:3 (see sequence search results). Stalker et al also teach cotton plants transformed via *Agrobacterium*-mediated transformation with vectors and constructs comprising the promoter operably linked to gene of interest (pg 13-15 and claim 6). The cotton fiber specific promoter would inherently be exposed to its required stimulus in at least some of the transformed cotton fiber cells.

16. Claims 1-5, 8-9, 12-13 and 16-17 rejected under 35 U.S.C. 102(e) as being anticipated by Perera et al (US Patent 6,462,257, filed 1 June 1999).

Perera et al teach nucleic acids (SEQ ID NOs:1 and 5) that each comprise 37 contiguous

nucleotides of SEQ ID NO:3 (see sequence search report and claims 1-7). Perera et al also teach a method of using the promoters to express a heterologous nucleic acid in a plant by transformation of the plant with a construct comprising the promoter operably linked to the heterologous nucleic acid and exposing the cell to a stimulus that induces transcription from the promoter, and plants, including dicots, and seeds thereby obtained (claims 8-23 and column 7, lines 1-14). Nucleic acids are introduced into plants via vectors (column 6, lines 55-65).

***Claim Rejections - 35 USC § 103***

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perera et al (US Patent 6,462,257, filed 1 June 1999) in view of Gordon-Kamm et al (1990, Plant Cell 2:603-618).

The claims are drawn to promoters comprising 30 contiguous nucleotides of SEQ ID NO:3, a method of using the promoters to express a heterologous nucleic acid in a plant, including maize, constructs and vectors used in the method, and plants, cells and seeds thereby obtained.

The teachings of Perera et al are discussed above. Perera et al do not disclose maize plants transformed with constructs comprising the nucleic acid.

Gordon-Kamm et al teach transformation of maize (pg 604-606) and production of seed from the transformed plants (pg 609-610).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of expressing a heterologous nucleic acid in a plant as taught by Perera et al, to apply the method to maize plants as described in Gordon-Kamm et al. One of ordinary skill in the art would have been motivated to do so because of the economic importance of maize (Gordon-Kamm et al, pg 603, right column paragraph 1) and because of the desirability of expressing heterologous nucleic acids in specific plant tissues (Perera et al, column 2, line 54, to column 3, line 6)

***Conclusion***

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
February 21, 2003